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09/750,022	12/29/2000	Indu J. Isaacs	016777/0454	6419

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EXAMINER

KAM, CHIH MIN

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 02/05/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/750,022

Applicant(s)

ISAACS, INDU J.

Examiner

Chih-Min Kam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 27 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-54 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 36-42 is/are ~~allowed~~. *free of prior art*
- 6) ☒ Claim(s) 1-22, 31, 43-46 and 49-54 is/are rejected.
- 7) ☒ Claim(s) 23-30, 32-35, 47, 48 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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## **DETAILED ACTION**

### ***Status of the Claims***

1. Claims 1-54 are pending.

Applicants' amendment filed November 27, 2002 (Paper No. 8) is acknowledged.

Applicants' response has been fully considered. Claims 1, 14, 15 and 32 have been amended, and claims 1-54 are examined.

### ***Priority Document***

2. The priority document (United Kingdom 9930882.7, filed December 30, 1999) is acknowledged (Paper No. 9).

### **Objection Withdrawn**

3. The previous objection to claims 14, 15 and 32 is withdrawn in view of the amendment to the claim, and applicants' response at page 3 in Paper No. 8.

### **Rejection Withdrawn**

### ***Claim Rejections - 35 USC § 112***

4. The previous rejection of claims 1-54, under 35 U.S.C.112, second paragraph, is withdrawn in view of applicants' amendment to the claims, and applicants' response at pages 3-5 in Paper No. 8.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-10; 22, and 49-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knudsen *et al.* (WO 99/43361) in view of Makino *et al.* (U. S. Patent 4,985,244).

Knudsen *et al.* teach a pharmaceutical composition comprising a GLP-2 derivative or analog, an isotonic agent such as mannitol, a buffer of histidine or sodium phosphate, a pharmaceutical acceptable carrier, a preservative and a surfactant, where the solubility and stability of GLP-2 is improved and the pharmaceutical formulation has pH 6.9 if phosphate buffer is used (page 4, line 19-29; page 3, lines 24-25; claims 1-4 and 10). The reference also indicates the concentration of the GLP-2 derivative is more than 0.5 mg and less than 100 mg/ml (page 4, lines 9-12; page 13, lines 16-19; claims 5-8), the formulation can be obtained in lyophilized form (page 13, line 10; claim 22), and the pharmaceutical composition can be administered by injection or means of infusion pump to treat small bowel syndrome or intestinal inflammation (page 12, lines 13-16; page 13, 16-24, claims 49-54). However, Knudsen *et al.* do not disclose using histidine as a stabilizing agent. Makino *et al.* disclose using 5% (w/v%) of histidine as a stabilizing agent in a vaccine composition (column 1, lines 15-20), which is about 1% (claim 9). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use the pharmaceutical composition of GLP-2 analogs as indicated by Knudsen *et al.* with the addition of a stabilizing agent taught by Makino *et al.* to treat a gastrointestinal disease because the addition of histidine can further improve the stability of the pharmaceutical formulation. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

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7. Claims 11, 12 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knudsen *et al.* in view of Makino *et al.* as applied to claims 1-10 above, further in view of Hora *et al.* (U. S. Patent 5,997,856).

Knudsen *et al.* teach a pharmaceutical composition comprising a GLP-2 derivative or analog, an isotonic agent such as mannitol, a buffer of histidine or sodium phosphate, a pharmaceutical acceptable carrier, a preservative and a surfactant, where the solubility and stability of GLP-2 is improved and the pharmaceutical formulation has pH 6.9 if phosphate buffer is used (page 4, line 19-29; page 3, lines 24-25; claims 1-4 and 10), the concentration of the GLP-2 derivative is more than 0.5 mg and less than 100 mg/ml (page 4, lines 9-12; page 13, lines 16-19; claims 5-8), and Makino *et al.* disclose using 5% (w/v%) of histidine as a stabilizing agent in a vaccine composition (column 1, lines 15-20), which is about 1% (claim 9). However, Knudsen *et al.* and Makino *et al.* do not disclose the concentration of mannitol in the pharmaceutical composition. Hora *et al.* disclose 1-5% mannitol is used as a bulking agent in a protein preparation (column 25, lines 7-14). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art using the pharmaceutical formulation of GLP-2 analogs as indicated by Knudsen *et al.* and Makino *et al.* with a known concentration of mannitol taught by Hora *et al.* (claims 11, 12 and 31) to treat a gastrointestinal disease because the addition of a known concentration of mannitol can further improve the stability of the pharmaceutical composition. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

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7. Claims 13-15 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knudsen *et al.* in view of Makino *et al.* as applied to claim 1 above, further in view of Drucker *et al.* (WO 97/39031).

Knudsen *et al.* teach a pharmaceutical composition comprising a GLP-2 derivative or analog, an isotonic agent such as mannitol, a buffer of histidine or sodium phosphate, a pharmaceutical acceptable carrier, a preservative and a surfactant, where the solubility and stability of GLP-2 is improved and the pharmaceutical formulation has pH 6.9 if phosphate buffer is used (page 4, line 19-29; page 3, lines 24-25; claim 1), and Makino *et al.* disclose using histidine as a stabilizing agent in a vaccine composition (column 1, lines 15-20). However, Knudsen *et al.* and Makino *et al.* do not disclose the source and the sequences of GLP-2, the h[Gly2]GLP-2 analog, and DPP-IV-resistant GLP-2 analogs. Drucker *et al.* disclose the sequence of human GLP-2, h[Gly2]GLP-2 analog, and DPP-IV-resistant GLP-2 analogs, where the Ala at position 2 has been modified (page 7, lines 8-20; page 9, lines 11-22, Table 1). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art using the GLP-2 analogs taught by Drucker *et al.* to prepare the pharmaceutical composition as indicated by Knudsen *et al.* and Makino *et al.* (claims 13-15 and 17-20) to treat a gastrointestinal disease because the use of DPP-IV resistant GLP-2 analogs in the pharmaceutical composition would result in a more stable pharmaceutical composition in vivo, where the GLP-2 analogs are degraded more slowly in vivo condition. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

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8. Claims 16 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knudsen *et al.* in view of Makino *et al.* as applied to claim 1 above, further in view of Thim *et al.* (U.S. Patent 5,912,229).

Knudsen *et al.* teach a pharmaceutical composition comprising a GLP-2 derivative or analog, an isotonic agent such as mannitol, a buffer of histidine or sodium phosphate, a pharmaceutical acceptable carrier, a preservative and a surfactant, where the solubility and stability of GLP-2 is improved and the pharmaceutical formulation has pH 6.9 if phosphate buffer is used (page 4, line 19-29; page 3, lines 24-25; claim 1), and Makino *et al.* disclose using histidine as a stabilizing agent in a vaccine composition (column 1, lines 15-20). However, Knudsen *et al.* and Makino *et al.* do not disclose the use of GLP-2 receptor to identify peptides that bind GLP-2 receptor or as GLP-2 receptor antagonist. Thim *et al.* disclose a GLP-2 receptor is identified and cloned, and a cell line stably expressing the receptor is used in a screening assay to identify the antagonist of GLP-2 receptor (column 10, lines 43-59). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art using the GLP-2 analogs taught by Thim *et al.* to prepare the pharmaceutical composition as indicated by Knudsen *et al.* and Makino *et al.* (claims 16 and 21) to treat a GLP-2 receptor-associated disease because the GLP-2 receptor antagonist can be used to treat GLP-2 receptor-associated diseases. Thus, the combined references result in the claimed invention and was, as a whole, *prima facie* obvious at the time the claimed invention was made.

9. Claims 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knudsen *et al.* in view of Makino *et al.* as applied to claim 1 above, further in view of Drucker (U. S. Patent 5,952,301).

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Knudsen *et al.* teach a pharmaceutical composition comprising a GLP-2 derivative or analog, an isotonic agent such as mannitol, a buffer of histidine or sodium phosphate, a pharmaceutical acceptable carrier, a preservative and a surfactant, where the solubility and stability of GLP-2 is improved and the pharmaceutical formulation has pH 6.9 if phosphate buffer is used (page 4, line 19-29; page 3, lines 24-25; claim 1), and Makino *et al.* disclose using histidine as a stabilizing agent in a vaccine composition (column 1, lines 15-20). However, Knudsen *et al.* and Makino *et al.* do not disclose a kit comprising a lyophilized GLP-2 formulation. Drucker disclose a kit comprising GLP-2 or GLP-2 analogs (column 2, lines 56-61). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art using the pharmaceutical composition as indicated by Knudsen *et al.* and Makino *et al.* to prepare a kit as taught by Drucker (claims 43-46) to treat a gastrointestinal disease because the kit containing the pharmaceutical composition can be used more conveniently in the treatment. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

10. Claims 23-30, 32-35, 47 and 48 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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*Conclusion*

11. Claims 1-22, 31, 43-46 and 49-54 are rejected, and claims 23-30, 32-35, 47 and 48 are objected. It appears that claims 36-42 are free of prior art.

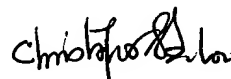
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. *CMK*  
Patent Examiner

February 1, 2002



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